Viscosity and Density of Lactulose Solutions[1]

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ABSTRACT

The density and viscosity of solutions of lactulose and solutions of lactulose and boric acid were determined using calibrated viscometers and a nominal 10-ml pycnometer, respectively. These data were necessary for the development of the recovery section of a continuous pilot plant process to produce lactulose, a valuable pharmaceutical, from lactose.
(**Key words**: viscosity, density, lactulose, boric acid)

Abbreviation key: DWB = dry weight basis.

INTRODUCTION

Lactulose is a noncaloric, complex carbohydrate that is highly valued as a pharmaceutical with worldwide markets. The principal worldwide outlets are as a laxative and for treatment of portal systemic encephalopathy. Lactulose is also used in infant formulas and as a health food because it induces growth of nonpathogenic bacteria in the colon.

Lactulose is normally synthesized by the isomerization of lactose. Recent methods for producing lactulose involve the use of complexation reagents. Hicks (2, 3, 4) showed that treatment of lactose with boric acid in a molar ratio of 1:1 (vol/vol) in the presence of tertiary amines or NaOH produces high yields of lactulose.

A commercially feasible process has been developed to produce lactulose based upon the use of boric acid and NaOH (5, 6, 7). A critical unit operation in the separation section of the process is evaporation to concentrate the solids (lactulose, lactose, boric acid, galactose, and tagatose). It is then possible to crystallize most of the boric acid and to filter it from the solution. During evaporation, the solution becomes quite viscous and dense. To design, operate, and control the evaporator properly, data on physical properties were needed, specifically, the viscosity and den-

sity of lactulose and lactulose plus boric acid solutions in water.

MATERIALS AND METHODS

Buma (1) reported the viscosity and density of concentrated lactose solutions. He used the Oswald viscometer that is valid for Newtonian fluids. Those data agreed with earlier published data on lactose. Considering this information, it was reasonable to assume that lactulose solutions would also be Newtonian. Therefore, calibrated Cannon-Fenske kinematic viscometers (Cannon Instrument Co., State College, PA) were used for viscosity determinations, and a nominal 10-ml pycnometer was calibrated with deionized water. Solutions were prepared by weighing the solid and adding sufficient deionized water to achieve the desired concentration. Each solution was immersed in a constant temperature water bath or suspended in ambient air for at least 1 h before the viscosity or density was measured. Concentration of lactulose solutions ranged from 20 to 76% solids; a 76% solution is the practical limit to solubility of lactulose in water. Solutions of lactulose and boric acid ranged from 9 to 39% solids containing 5, 10, or 15% boric acid, dry weight basis (**DWB**). The presence of boric acid limits the solubility of lactulose in this solution.

Lactulose (Sigma Chemical Co., St. Louis, MO) had a purity of approximately 98%. Boric acid was NF granular and conformed to all standards of The National Formulary (9). The boric acid was supplied by U. S. Borax and Chemical Corp. (Los Angeles, CA). Temperature measurements were made with a Natural Bureau of Standards calibrated thermometer that had a range of −1 to 50°C and graduations of 0.1°C.

RESULTS

The viscosities of lactulose solutions are shown in Figure 1. The data were plotted as the natural log of viscosity versus the reciprocal of the absolute temperature to obtain linear correlations and also to fit the broad range of viscosity data on a reasonable scale. The data closely fit the straight lines as shown in the figure. Correlation coefficients were 0.99 or higher.

For process design, a correlation was needed that included the effect of concentration. The empirical correlation (8) presented in Equations [1] to [3] fit the data with a correlation coefficient of 0.996.

$$\mu = 10^{-6} \exp[A\ (1/T) + B] \qquad [1]$$

$$A = 5.84(10^6)\ \exp[-511/(\text{percentage of solids})] - 3.87(10^4)/(\text{percentage of solids}) + 4107 \qquad [2]$$

$$B = -2.43(10^4)\ \exp[-552/(\text{percentage of solids})] + 76.7/(\text{percentage of solids}) - 10.6 \qquad [3]$$

where μ = kinematic viscosity (square meters per second), A and B = empirical constants, and 10^{-6} = SI conversion factor.

Figure 2 presents the viscosity of solutions of lactulose and boric acid at 5, 10, and 15% boric acid (DWB). Although the data files were readily fit with Equation [1], a correlation was needed that included the effect of concentration for process calculations. The empirical fit developed (shown in Equations [4] to [6]) applies for solutions of 9 to 39% solids containing 5 to 15% boric acid (DWB). In this range, the viscosity at the different percentages of boric acid were indistinguishable. The correlation coefficient was 0.967. Equation [4] also gives reasonable predictions for the viscosity of lactulose solutions with no boric acid up to 40% total solids.

$$\mu = 10^{-6} \exp[A(1/T) + B] \qquad [4]$$

$$A = 24.4\ (\text{percentage of solids}) + 1789 \qquad [5]$$

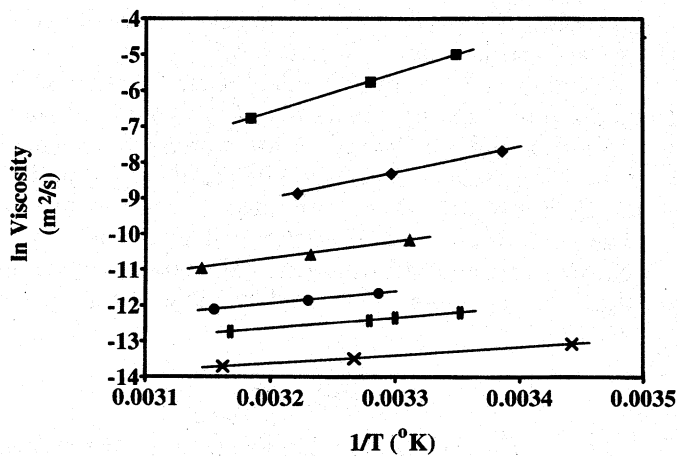$$B = -0.0397\ (\text{percentage of solids}) - 6.29 \qquad [6]$$

Figure 1. Viscosity of lactulose solutions at different temperatures (T). Lactulose concentrations: 76.0% (■), 69.8% (♦), 59.1% (▲), 49.1% (●), 40% (||), and 20.0% (X).
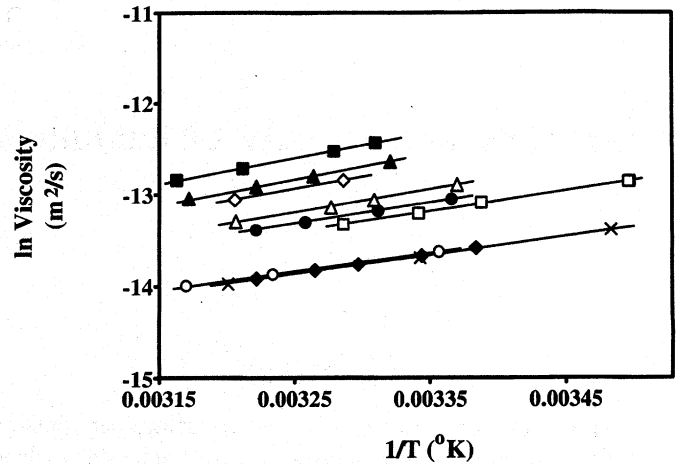

Figure 2. Viscosity of solutions of boric acid and lactulose at different temperatures (T). Concentrations: 5% boric acid, and 10% solids (♦), 25% solids (●), or 35% solids (▲); 10% boric acid and 10% solids (o), 28% solids (△), or 39% solids (■); and 15% boric acid and 9% solids (X), 25% solids (□), or 35% solids (◊).

where T is absolute temperature (Kelvin degrees).

The data of Buma (1) were also correlated with Equation [1] at each of four solids concentrations. The values of A and B were determined by regression at each solids concentration (Table 1). Good fit was evidenced by a correlation coefficient of 0.9992. The densities of lactulose solutions from 20 to 76% solids were measured over the temperature range of 22 to 45°C. Variation in density was minimal over this temperature range relative to concentration; therefore, density data were plotted for all temperatures versus concentration (Figure 3). The densities of solutions of boric acid and lactulose from 9 to 39% total solids were measured for 5, 10, and 15% boric acid (DWB) over the temperature range of 19 to 40°C. Again, variation in density was minimal over this temperature range relative to concentration. These density data were plotted for all temperatures versus concentration of total solids (Figure 3).

TABLE 1. Values of coefficients in Equation [1] for lactose.[1]

Solids	A	B
(%)		
10	1710.89	−5.53
20	2044.56	−6.27
30	2421.24	−7.04
40	2926.70	−8.04

[1]$\mu = 10^{-6} \exp[A(1/T) + B]$, where μ = kinematic viscosity (square meters per second), A and B = empirical constants, and 10^{-6} = SI conversion factor.
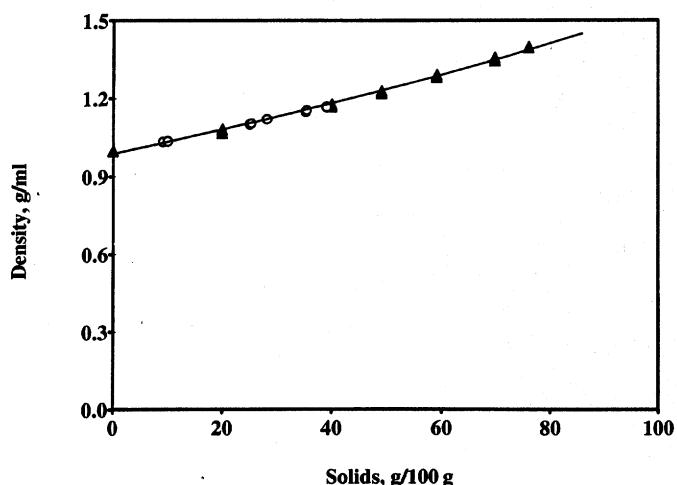
Figure 3. Densities of lactulose solutions (▲) and solutions of boric acid and lactulose (○).

Within experimental error, both data files fell on the same curve, and the data showed a slight curvature. An exponential equation was selected to correlate the combined data as presented in Equation [7]. The correlation coefficient was 0.996.

$$\rho = \exp[0.00441 \text{ (percentage of solids)} - 0.01] \quad [7]$$

where ρ = density gradient (grams per milliliter).

These data were used as part of a study (5, 6) to develop a process for converting lactose to lactulose using boric acid as a complexation agent. Specifically, the data were used for developing the separation section consisting of a crystallizer and evaporator (7). It was in these units that knowledge of the solution viscosity and density was critical to successful control of the process.

CONCLUSIONS

Kinematic viscosity and density of solutions of lactulose and of lactulose and boric acid were determined and correlated. The density of solutions of lactulose and of lactulose and boric acid are essentially identical and are an exponential function of solids content. At equal solids content, the viscosity of solutions of lactulose is greater than of lactulose and boric acid. A standard exponential equation correlates kinematic viscosity with solids content and reciprocal of absolute temperature. At equal solids content, there is little difference in these physical properties between 5 and 15% boric acid. The correlations are sufficiently accurate for process design.

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